REMARKS

Claims 1, 4-6, 10, 16-18 and 20-32 are pending and under consideration.

Rejection under 35 U.S.C. § 102(b) is in Error

Claims 1, 4-6, 10, 16-18, 20 and 22-32 are rejected under 35 U.S.C. § 102(b) as, allegedly, anticipated by International Patent Publication No. WO 92/15285 by Lentz *et al.* ("Lentz"). According to the Examiner, although the disclosed release profiles only show drug release up to a period of 24 hours, the amount of drug released in some figures remains under 100%, therefore, the instant claims are anticipated.

Applicants disagree and point out that in order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). "Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. . ." *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707 (Fed. Cir. 1984). None of the pending claims is explicitly anticipated by the disclosure of Lentz. First, Applicants note that presently pending claims relate to a method for producing a controlled release matrix, which method requires a co-extrusion of a dry mixture of starch and a pharmaceutically active agent at a die temperature below 100°C under normal pressure, and wherein the co-extruding is under sheer force, temperature and pressure conditions such that the resulting product is vitrified, and to controlled release matricies produced by the method. The only example in Lentz which co-extrudes starch and an active agent, *i.e.*, Example 18, leads to a foamed product, not a vitrified product. Thus, Lentz does not anticipate the claimed compositions and methods.

Furthermore, if the Examiner is alleging that the compositions of the present invention are allegedly anticipated by Lentz's compositions comprising separately processed starch (MDS) mixed with an active agent, Applicants submit that the Examiner is improperly combining one teaching of Lentz with regard to processing starch and combining the processed starch with an active agent and the teaching in Lentz with regard to co-extruding previously processed starch with an active agent.

Even if the Examiner alleges that the tablet resulting from combining the processed starch (MDS) with an active agent is the same as the claimed co-extruded compounds of the present invention, Applicants point out that this allegation is in error, since the claimed co-extruded compounds are different from the combined product of Lentz. Lentz discloses compositions comprising (i) a matrix comprising starch having been processed under shear at

temperatures of about 80°C to 240°C in a closed volume wherein the water content of the matrix was maintained at about 5% to about 45% by weight based on the starch/water mix, and (ii) an active ingredient. Preferably, the starch is processed to a specific endothermic transition just prior to oxidation and thermal degradation. Note that the active ingredient is not processed with the starch but is merely combined with the starch after processing. *See* Lentz at page 11, lines 13-25; at page 14, lines 16-25. Moreover, the processed starch in Lentz, called molecularly dispersed starch or MDS, is not stiff or glassy, but, rather, is soft and rubbery, which allows the extruded MDS to be more compressible. *See* Lentz at page 28, lines 31-38, which teaches that the MDS obtained by extrusion is soft and rubbery. Even though both Lentz and the present invention teach destructurization of starch by way of extrusion, the nature of the destructured starch obtained is different since the molecularly dispersed starch of Lentz is soft and rubbery and, thus, above glass transition temperature. In fact, Lentz teaches at page 14, lines 6-25, that it is preferred that the process heats the starch above the glass transition temperature.

In contrast, the extruded matrices obtained by the present invention are vitrified, *i.e.*, rigid and, thus, their temperature never exceeded the glass transition temperature and preferably remains below the glass transition temperature.

Thus, Applicants submit that not only is the sole co-extruded composition of Lentz different from the claimed co-extruded compositions of the present invention, but the products of Lentz resulting from combining already processed starch with an active agent are also different, since in each instance, the starches are different. Applicants note that the fact that Lentz's compositions may also follow the lapidus function is immaterial to the present analysis since the compositions (and methods) claimed in the instant specification are different from those taught by Lentz. Lentz cannot anticipate the claimed invention as a matter of law and fact because the compositions taught therein are different from the claimed compositions.

In view of the foregoing, Applicants submit that the claimed co-extruded compositions and co-extrusion methods are not anticipated by Lentz, and, therefore, respectfully request that this rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a) is in Error

Claims 1, 4-6, 10, 16-18 and 20-32 remain rejected under 35 U.S.C. § 103(a), as, allegedly, obvious over International Patent Publication No. WO 92/15285 by Lentz *et al.* ("Lentz"). According to the Examiner, Applicants previous response does not overcome the

rejection as the response is based on a narrow interpretation of Lentz. Applicants respectfully disagree with the Examiner.

Preliminarily, Applicants, in order not to burden the record, hereby incorporate by reference the remarks made in the last response with regard to the teachings of Lentz including the Declaration of Dr. Rein and present the following additional arguments.

Applicants point out that the Examiner's contention that there is an overlap of temperatures between the extrusion method of the present invention and the method disclosed in Lentz is incorrect. Applicants respectfully note that the Examiner is mistaken as to the application of MPEP §§ 2111 and 2123. MPEP § 2111 refers to the claims of the application pending before the U.S. Patent and Trademark Office, not to any teaching in the prior art. The Examiner seems to be taking the adage of "broadest reasonable interpretation" and applying it to the teaching of Lentz rather than to the currently pending claims. The pending claims are clearly directed to co-extrusion at a die temperature of less than 100°C under normal pressure. MPEP § 2123 indeed states that one must look to the entire disclosure of a prior art patent, not just to disclosed embodiments; however, MPEP § 2123 does not mean that an Examiner can reasonably create a teaching by extrapolating a disclosed embodiment to a broader teaching, without any further guidance from the reference itself.

As submitted previously, the teaching of Lentz regarding the temperature range of 80°C to 240°C for processing does not mean that the processing can take place at any temperature between 80°C to 240°C but rather means that the entire process occurs at temperatures encompassing 80°C to 240°C, never just at 80°C or 130°C or 240°C. One skilled in the art of extrusion would clearly understand that Lentz is giving the range of the temperatures of the extruder, which temperatures differ at different locations of the extruder. Lentz specifically teaches on page 28, lines 17-19 that the extruder barrel temperature profile was 80°C - 160°C - 240°C (for feed, screw and die, respectively). One skilled in the art would understand that the temperature of the extruder orifice (die) is 240°C. This is an important distinction between the teachings of Lentz and the presently claimed invention, where the orifice of the extruder is below 100°C, which also means that all other parts of the extruder are below 100°C.

The only passage in Lentz that concerns co-extrusion of a pharmaceutically active agent and a starch is on page 17, line 37 to page 18, line 1. However, there are absolutely no details in the Lentz specification to teach one skilled in the art how such a co-extrusion can be carried out, unless the co-extrusion is carried out by the same methodology as Lentz uses to extruded the starch alone. Example 18 in Lentz, however, does provide details for a method of co-extrusion. However, Example 18 teaches co-extrusion of not starch but molecularly dispersed starch

(which was previously extruded starch) with an active agent (clotrimazole) and talc. Further, as explicitly stated by Lentz, the resulting co-extruded product is a foamed, rubbery product, which is not a controlled release matrix. The pending claims require that the matrix produced by the method be a vitrified controlled release matrix, *i.e.*, glassy. A foamed, rubbery product is not a glassy vitrified product. Applicants do not find it reasonable to interpret the disclosure of Lentz to include the teaching or suggestion of a controlled-release product produced by co-extrusion below 100°C. Lentz does not teach or suggest a modification of its disclosed method requiring that the temperature at the orifice of the extruder (as well as all other parts of the extruder) during the extrusion process be below 100°C under normal pressure. Lentz does not teach or suggest that the temperature be kept under 100°C, and the only time Lentz actually co-extruded an active agent with its molecularly dispersed starch, no controlled release product was achieved. Indeed, the only disclosed specific experimental conditions for processing starch are found in Example 1 of Lentz and the molecularly dispersed starch (MDS) produced in Example 1 is used throughout all other experiments, including the co-extrusion experiment in Example 18. Applicants submit that the MDS produced according to Example 1 is, indeed, representative of the MDS used in all other experiments disclosed in Lentz, which MDS is not the same as nor suggestive of the co-extruded compositions of the present invention. Applicants submit that it is unreasonable for the Examiner to extrapolate the disclosure of Lentz to suggest the co-extrusion of starch and an active agent at a die temperature of less than 100°C.

With regard to the Examiner's reference to Example 11 and extrusion of starch at 70°C, Applicants note that in Example 11 the preferred temperature range for producing MDS is 110°C to about 170°C, *i.e.*, above 100°C, and that the comparative reference to 70°C starch matrix forms produced by processing the already processed starch (MDS) at 70°C, does not provide any additional teaching or suggestion of the co-extrusion of native starch and an active agent at a die temperature of less than 100°C under normal pressure.

With regard to the Examiner's allegation that the Declaration of Dr. Rein does not fully support the full breadth of the claims, Applicants note that experiments disclosed in the present specification as originally filed provide a temperature profile of 65°C-80°C-98°C, thus encompassing a die temperature of under 100°C. Furthermore, Applicants note that Dr. Rein not only performed an experiment with a temperature profile 80°C-80°C-80°C, but also performed experiments with die temperatures of 97°C, 100°C, 102°C, and 114°C. Thus, the specification as originally filed already provides examples covering co-extrusion at a die temperature of less than 100°C and Dr. Rein subsequently showed by the submitted experimental data that, if one were to co-extrude at a die temperature of less than 100°C, one would obtain vitrified products

with controlled release properties. Thus, evidence has been presented that covers the full breadth of the claims.

In view of the foregoing, Applicants respectfully request that the rejection under Section 103(a) in view of Lentz be withdrawn.

CONCLUSION

Applicants respectfully request that the above-made remarks of the present response be entered and made of record in the file history present application. Applicants submit that the presently pending claims meet all requirements for patentability and respectfully request allowance and action for issuance.

Applicants request that the Examiner call the undersigned at (212) 326-3921 if any questions or issues remain.

Respectfully submitted,

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